in 50% formamide, 5 x SSC, and 1% SDS at 42°C, or incubation in 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS at 65°C.

8. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, the nucleic acid comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:3.

9. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, wherein the complement of the nucleic acid specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:1, wherein said stringent conditions comprise incubation in 50% formamide, 5 x SSC, and 1% SDS at 42°C, or incubation in 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS at 65°C.

REMARKS

I. Status of the Claims

Claims 1-40 were originally filed. Claims 1-9, 19, and 20 are currently under examination as the result of a restriction requirement. The phrase "cyclic nucleotide gated cation channel" is inserted into claims 1, 7, and 8 to address an objection to informality. This recitation of the full name of CNG finds support in the specification, *e.g.*, on page 1 line 22. Claims 5-7 and 9 are amended to recite specific hybridization conditions, support for which can be found on page 22 lines 10-12, lines 17-19, and lines 25-32. In addition, claim 9 as amended now recites a nucleic acid encoding a CNG2B polypeptide, which is supported throughout the specification including claim 7 as originally filed. Amended claim 9 also recites the complementary strand of a nucleic acid. This is an aspect encompassed by the definition of "nucleic acid" given on page 14 lines 13-14, since a "nucleic acid" can be in either single- or double-stranded form. Thus, no new matter is introduced by the present amendment.

II. Election of Species

Applicants hereby acknowledge the provisional species election of SEQ ID NOs:12 and 13 to prosecute claim 5. The election was made with traverse.

III. Objections

Claims 1, 7, and 8 were objected to because of the recitation of "CNG" or "CNG2B." As amended, these claims now recite the full name of "cyclic nucleotide gated cation channel."

Claim 5 was objected to for reciting non-elected nucleotide sequences. The present amendment has addressed this issue.

IV. Claim Rejections

A. 35 USC §101

Claims 1-9, 19, and 20 were rejected under 35 USC §101 for alleged lack of a "substantial" or "real world" utility. Applicants respectfully traverse the rejections.

Prediction of Orthologous Polypeptide Function Based on High Level of Overall Sequence Homology Is Reliable

The pending claims are directed to nucleic acids encoding a CNG2B polypeptide or a subunit of a CNG cation channel. As the Examiner has acknowledged, human CNG2B gene shows significant sequence homology to rat OCNC2 gene, a gene known to form functional heteromultimeric ion channels that are involved in rat olfactory signal transduction. Particularly noteworthy is that the amino acid sequence of human CNG2B is more than 93% identical to that of rat OCNC2, which makes the rat polypeptide much more homologous to human CNG2B than any other known ion channels. This fact, combined with the observation that the two genes have similar expression patterns (both expressed in the brain), demonstrates to those of skill in the art that CNG2B is the human ortholog of the rat gene and has similar biological functions. See page 62 line 20 to page 63 line 15 of the specification.

The Examiner raised the concern that prediction of a CNGB2 polypeptide function based on sequence homology may not be reliable in light of the diversity of structure and function of CNG ion channels. Applicants respectfully note that the predictability of a polypeptide function largely depends on the level of sequence homology the polypeptide shares with another polypeptide with known functions. Citing the article by Bork and Koonin, the Examiner appears to be of the opinion that a protein's function cannot be predicted based on its sequence homology to another protein. Yet a closer look at the examples given in the Bork and Koonin reference reveals that erroneous conclusions in predicting protein functions are the results of making such predictions relying on ***sequence homology within a region of the protein***, which has a limited overall sequence homology to a known protein. *See, e.g.*, page 315 left column last paragraph regarding mis-annotation of a protein as a kinase due the presence of an SH3 domain; page 317 left column first full paragraph regarding the ortholog / paralog confusion of p53 homologs based on sequence homology in a C-terminal SAM domain. This is further evidenced by the contrast between Figure 2 of the Bork and Koonin reference, which shows a sequence comparison window of about 70 amino acids and low levels of amino acid identity, and Figure 1 of the present application, which shows the alignment of full length human CNG2B polypeptide and rat OCNC2 polypeptide in 575 amino acids and a greater than 93% overall sequence identity.

The present application relies on a high level of overall sequence identity and similar expression pattern to conclude that human CNG2B is the ortholog of rat OCNC2 and thus possesses similar biological functions. This methodology for identifying orthologs of proteins with known functions is well established and frequently used by those skilled in the art. This methodology is also fundamentally differently from the methods of predicting protein functions as described in the references the Examiner cited in the Action. An artisan will agree that with such a striking overall sequence identity, human CNG2B is likely to perform a biological role significantly similar to that of rat OCNC2.

The present application provides evidence to support the conclusion that human CNG2B is the ortholog of rat OCNC2 and functions similarly (see the bridging sentence between pages 62 and 63). Unless the Examiner has any evidence or reason to doubt or refute the conclusion, Applicants submit that the utility requirement is satisfied.

Claims Directed to Fully Characterized Proteins or Encoding Nucleic Acids Meet the Utility Requirements of 35 USC §101

Claims directed to CNG2B ion channel nucleic acids meet the utility requirements of 35 USC §101 for another reason. The claimed CNG2B nucleic acids are fully characterized both structurally and functionally. The nucleic acid sequences are claimed by reference to shared structural features, *e.g.*, encoding a polypeptide with a percent identity to the amino acid sequence disclosed in SEQ ID NO:1. The CNG2B nucleic acids are also claimed by reference to shared functional features, *e.g.*, encoding a CNG2B polypeptide.

According to the recently promulgated "Guidelines for Examination of Applications for Compliance with the Utility Requirement," a characterized protein has utility. This standard is made evident from Example 8 of the guidelines. In Example 8, a compound A is disclosed to inhibit enzyme XYZ, a well known enzyme, *in vitro*. The specification states that the compound A can be used to treat diseases caused or exacerbated by enzyme XYZ. No such diseases are named. Claim 1 is directed to compound A. Claim 2 is directed to a method of treating a disease caused or exacerbated by enzyme XYZ consisting of administering an effective amount of compound A to a patient. In the subsequent analysis, claim 2 is deemed to be insufficiently supported by a real world context of use. This is because neither the specification nor the art of record discloses any disease or conditions caused or exacerbated by enzyme XYZ and therefore, the asserted utility is seen as a method of treating an unspecified and undisclosed disease or condition, which does not define a "real world" context of use. Claim 1, however, is regarded as having utility because claim 1 is directed to a compound that inhibits an

enzyme and enzymes have well established utility in the art, i.e., catalyzing certain reactions.

This example can be compared to the present application. The present application claims a nucleic acid that encodes, *e.g.*, a CNG2B ion channel, which is analogous to compound A that inhibits enzyme XYZ. The specification states that CNG2B ion channel is likely involved in olfactory signal transduction. Thus, the ion channel can be used to as a target for treating disorders related to olfactory signaling. In Example 8, claim 1 directed to compound A is found to have utility even though there is no disclosure of specified disease that to be treated. Accordingly, even if the Examiner is not convinced, despite the disclosure by the present specification and the general belief held by those of skill in the art, that CNG2B is involved in olfactory signal transduction, a claim directed to compound A, i.e., the nucleic acid in the present case, has utility. The claimed nucleic acids have utility because they encode CNG2B cation channels or CNG ion channel subunits, which, like enzymes, have a well established utility in the art: adjusting the passage of ions according to varying conditions. Applicants therefore respectfully request that the rejections be withdrawn.

B. 35 USC §112 First Paragraph: Enablement

Claims 1-9, 19, and 20 were rejected under 35 USC §112 first paragraph. According to the Examiner, since the application fails to provide a real world utility for the invention, one skilled in the art will not know how to use the invention, the invention thus necessarily fails the enablement test. In light of the forgoing discussion, Applicants submit a real world utility is established and the enablement rejections associated with lack of utility are traversed.

The Examiner further stated that even if a patentable utility was shown, the disclosure was not fully enabling for the scope of the pending claims. Applicants respectfully traverse the rejections.

A claimed invention is enabled when the disclosure allows one of ordinary skill in the art to make and use the invention without undue experimentation. MPEP §2164.01. The test for enablement is set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). The consideration of multiple factors is necessary: the breadth of the claims; the nature of the invention; the state of the prior art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In the present case, the claims are directed to nucleic acids encoding a subunit of a CNG2B cation channel with a well-defined structure and readily testable functional feature. Working examples of human CNG2B coding sequence and amino acid sequence are provided. The specification also contains ample directions to practice the invention, such as methods of cloning CNG2B nucleic acid sequences (*see, e.g.*, page 26 line 20 to page 29 line 13), expression of CNG2B nucleic acid sequences (*see, e.g.*, page 29 line 15 to page 31 line 30), purifications of CNG2B polypeptides (*see, e.g.*, page 32 line 1 to page 34 line 32), immunological detection of CNG2B polypeptides (*see, e.g.*, page 35 line 1 to page 42 line 11), and assays for modulators of CNG2B (*see, e.g.*, page 42 line 13 to page 50 line 34). The level of technical sophistication is high in the art, and the CNG2B cation channel variants can be readily tested according to the methods commonly used by those skilled in the art or the methods taught by the specification (such as nucleic acid or amino acid sequence comparison, nucleic acid hybridization assays, and assays for ion channels with the characteristics of cyclic nucleotide-gating) to eliminate inoperable embodiments. MPEP §2164.01 states, complex experimentation is not necessarily undue, if the art typically engages in such experimentation. In the present case, although some experimentation may be involved to practice the invention using embodiments other than those specifically described in the application, such experimentation utilizes well-established techniques and is routinely conducted in the art. Thus, the experimentation does not constitute undue experimentation.

In summary, Applicants believe that the disclosure by the present application is sufficiently enabling for a person with ordinary skill in the art to practice the invention and that no undue experimentation is required. The rejections for inadequate enablement should thus be properly withdrawn.

C. 35 USC §112 First Paragraph: Written Description

Claims 1, 3, 8, 19, and 20 were rejected under 35 USC §112 for alleged inadequate written description. Applicants respectfully traverse the rejections.

The pending claims as amended fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Finally, the MPEP states that structural formulas provide a convenient method of demonstrating possession of specific molecules, MPEP 2163.

With regard to the claimed nucleic acids, claims 1 and 8 (and hence claims 3, 19, and 20, which depend from claim 1) set forth both functional elements, *e.g.*, encoding a cyclic nucleotide gated cation channel CNG2B or a subunit of a cation channel, as well as structural elements, *e.g.*, having a certain percentage sequence identity to a reference nucleotide sequence or encoding a polypeptide having a certain percentage sequence identity to a reference amino acid sequence. Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared functional and structural properties.

The nucleotide sequence of a nucleic acid, such as a DNA molecule, is a physical/structural property of the molecule, *see, e.g.*, Stryer, *Biochemistry*, pages 72-73

(3rd ed. 1988), attached as Exhibit 1. Thus, it is also a physical/structural property of a nucleic acid to have a certain percentage sequence identity to a reference nucleotide sequence, or to encode a polypeptide having an amino acid sequence with a certain percentage sequence identity to a reference amino acid sequence, because such percentage identity, either in nucleotide sequence or in amino acid sequence of an encoded polypeptide, relies entirely upon the nucleotide sequence of the nucleic acid.

The functional features of the claimed nucleic acids are also provided: each encodes either a CNG2B polypeptide, or a subunit of a cation channel capable of forming, with at least one CNG alpha subunit, a cation channel with CNG characteristics. As required by the standard set forth in *University of California v. Eli Lilly,* these features are common to all members of the claimed genus.

Thus, both structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). As such, Applicants respectfully request that the Examiner withdraw the rejections.

D. 35 USC §112 Second Paragraph

Claims 5-7 and 9 were rejected under 35 USC §112 second paragraph for alleged indefiniteness. Specifically, the Examiner pointed to the recitation of "selectively hybridizes under stringent hybridization conditions," "selectively hybridizes under moderately stringent hybridization conditions," and "specifically hybridizing under stringent conditions" without giving the specific conditions as the cause of the alleged indefiniteness. Claims 5-7 and 9 as amended now recite specific hybridization conditions. Applicants thus submit the indefiniteness rejections are overcome.

E. 35 USC §102

Claim 9 was rejected under 35 USC §102(a) as allegedly being anticipated by Birren et al. (GenBank, Accession No. AC036216). Applicants respectfully traverse the rejections in light of the present amendment.

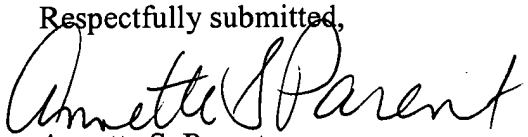
In order to anticipate a claim, a single reference must contain all elements of the claim. As amended, claim 9 now recites an isolated nucleic acid that encodes a CNG2B polypeptide and its complement can hybridize under specified conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:1. AC036216 consists of a polynucleotide of about 650 bp, which is less than an intact open reading frame (ORF) for a CNG2B polypeptide. In contrast, SEQ ID NO:3, the coding sequence of SEQ ID NO:1, consists of a complete ORF of about 1.8 kbp. AC036216 thus cannot encode a CNG2B ion channel. Without this element, this reference cannot anticipate claim 9 as amended. Applicants therefore respectfully request that the rejection for alleged anticipation by this disclosed sequence be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (once amended) An isolated nucleic acid encoding a polypeptide comprising a subunit of a cation channel, the polypeptide:

(i) forming, with at least one cyclic nucleotide gated cation channel (CNG) alpha subunit, a cation channel having the characteristic of cyclic nucleotide-gating; and

(ii) comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:1.

5. (once amended) The nucleic acid of claim 1, wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as the primers selected from the group consisting of:

[GCAGATCTTTCAGAACTGTGAGGCCA (SEQ ID NO:4)
CCTGCCCTCTTCATCTTTGGAAGTTC (SEQ ID NO:5)
GCCAACATCAAGAGCCTAGGTTATTC (SEQ ID NO:6)
GGATGATCTACAGACCAAGTTTGCTCG (SEQ ID NO:7)
ATGAGCCAGGACACCAAAGTGAAGAC (SEQ ID NO:8)
GTTGATGATGCTGATCTCCCCAAAG (SEQ ID NO:9)
GGATGATGAGGTTATACATGACTGGG (SEQ ID NO:10)
AGGCTAGCAACTTCCTGGCCTTGGAT (SEQ ID NO:11)]
GCGAAAGCTTCCACCATGAGCCAGGACACCAAAGTG (SEQ ID NO:12) and
CATGTCTAGAATGGGGATGGGGTCACTCTGGACCT (SEQ ID NO:13),

wherein the nucleic acid is amplified under hybridization conditions comprising a denaturation phase comprising incubation at 95°C for 2 min., an annealing

phase comprising incubation at 62°C for 2 min., and an extension phase comprising incubation at 72°C for 2 min.

6. (once amended) The nucleic acid of claim **1**, wherein the nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, wherein said moderately stringent hybridization conditions comprise incubation in 40% formamide, 1 M NaCl, and 1% SDS at 37°C with a wash in 1 x SSC at 45°C.

7. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, the nucleic acid specifically hybridizing under stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, wherein said stringent conditions comprise incubation in 50% formamide, 5 x SSC, and 1% SDS at 42°C, or incubation in 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS at 65°C.

8. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, the nucleic acid comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:3.

9. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, wherein the complement of the nucleic acid [that] specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:1.

APPENDIX B

ALL CLAIMS UNDER EXAMINATION UPON ENTRY OF AMENDMENT

1. (once amended) An isolated nucleic acid encoding a polypeptide comprising a subunit of a cation channel, the polypeptide:

(i) forming, with at least one cyclic nucleotide gated cation channel (CNG) alpha subunit, a cation channel having the characteristic of cyclic nucleotide-gating; and

(ii) comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:1.

2. (as filed) The nucleic acid of claim **1**, wherein the nucleic acid encodes a polypeptide comprising an amino acid sequence of SEQ ID NO:1.

3. (as filed) The nucleic acid of claim **1**, wherein the nucleic acid comprises a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:3.

4. (as filed) The nucleic acid of claim **3**, wherein the nucleic acid comprises a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3.

5. (once amended) The nucleic acid of claim **1**, wherein the nucleic acid is amplified by primers that selectively hybridize under stringent hybridization conditions to the same sequence as the primers selected from the group consisting of:

GCGAAAGCTTCCACCATGAGCCAGGACACCAAAGTG (SEQ ID NO:12) and

CATGTCTAGAATGGGGATGGGGTCACTCTGGACCT (SEQ ID NO:13),

wherein the nucleic acid is amplified under hybridization conditions comprising a denaturation phase comprising incubation at 95°C for 2 min., an annealing

phase comprising incubation at 62°C for 2 min., and an extension phase comprising incubation at 72°C for 2 min.

6. (once amended) The nucleic acid of claim 1, wherein the nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, wherein said moderately stringent hybridization conditions comprise incubation in 40% formamide, 1 M NaCl, and 1% SDS at 37°C with a wash in 1 x SSC at 45°C.

7. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, the nucleic acid specifically hybridizing under stringent conditions to a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2 or SEQ ID NO:3, wherein said stringent conditions comprise incubation in 50% formamide, 5 x SSC, and 1% SDS at 42°C, or incubation in 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS at 65°C.

8. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, the nucleic acid comprising a nucleotide sequence having at least 90% sequence identity to SEQ ID NO:2 or SEQ ID NO:3.

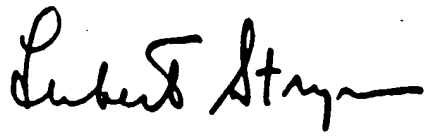
9. (once amended) An isolated nucleic acid encoding a cyclic nucleotide gated cation channel (CNG) 2B polypeptide, wherein the complement of the nucleic acid specifically hybridizes under stringent conditions to a nucleic acid encoding an amino acid sequence of SEQ ID NO:1, wherein said stringent conditions comprise incubation in 50% formamide, 5 x SSC, and 1% SDS at 42°C, or incubation in 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS at 65°C.

19. (as filed) An expression vector comprising the nucleic acid of claim 1.

20. (as filed) A host cell transfected with the vector of claim 19.

BIOCHEMISTRY

THIRD EDITION



LUBERT STRYER
STANFORD UNIVERSITY

W. H. FREEMAN AND COMPANY / NEW YORK

EXHIBIT 1

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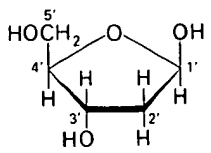
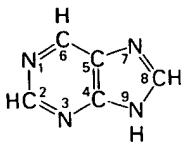
DNA CONSISTS OF FOUR KINDS OF BASES JOINED TO A SUGAR-PHOSPHATE BACKBONE

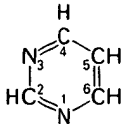
DNA is a polymer of deoxyribonucleotide units. A nucleotide consists of a nitrogenous base, a sugar, and one or more phosphate groups. The sugar in a deoxyribonucleotide is *deoxyribose*. The *deoxy* prefix indicates that this sugar lacks an oxygen atom that is present in ribose, the parent compound. The nitrogenous base is a derivative of *purine* or *pyrimidine*.



β-D-2-Deoxyribose

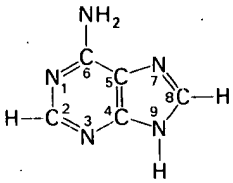


Purine

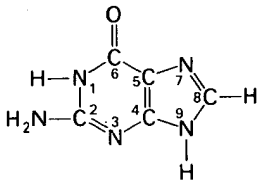


Pyrimidine

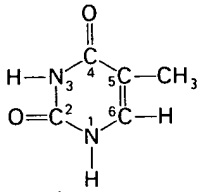
The purines in DNA are *adenine* (A) and *guanine* (G), and the pyrimidines are *thymine* (T) and *cytosine* (C).



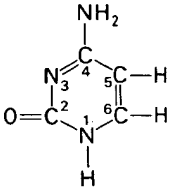
Adenine
(A)



Guanine
(G)

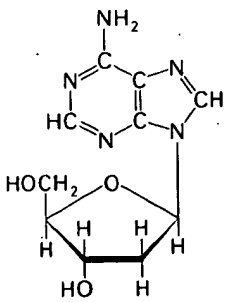


Thymine
(T)

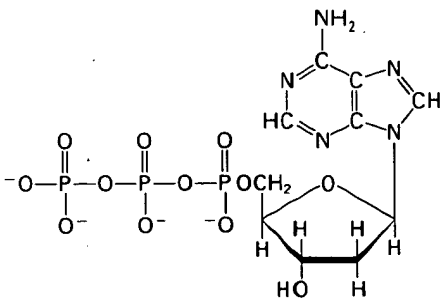


Cytosine
(C)

In a deoxyribonucleotide, the C-1 carbon atom of deoxyribose is bonded to N-1 of a pyrimidine or N-9 of a purine. The configuration of this *N*-glycosidic linkage is β (the base lies above the plane of the sugar ring). A *nucleoside* consists of a purine or pyrimidine base bonded to a sugar. The four nucleoside units in DNA are called *deoxyadenosine, deoxyguanosine, deoxythymidine,* and *deoxycytidine*. A *nucleotide* is a phosphate ester of a nucleoside. The most common site of esterification in naturally occurring nucleotides is the hydroxyl group attached to C-5 of the sugar. Such a compound is called a *nucleoside 5-phosphate* or a *5'-nucleotide*. For example, *deoxyadenosine 5'-triphosphate* (dATP) is an activated precursor in the synthesis of DNA. A primed number denotes an atom of the sugar, whereas an unprimed number denotes an atom of the purine or pyrimidine ring. The prefix *d* in dATP indicates that the sugar is deoxyribose to distinguish this compound from ATP, in which the sugar is ribose.



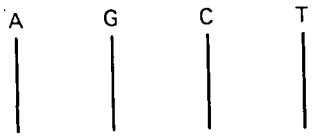
Deoxyadenosine
(A nucleoside)



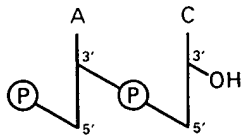
Deoxyadenosine 5'-triphosphate
(dATP)
(A nucleotide)

The *backbone* of DNA, which is invariant throughout the molecule, consists of deoxyriboses linked by phosphate groups. Specifically, the 3′-hydroxyl of the sugar moiety of one deoxyribonucleotide is joined to the 5′-hydroxyl of the adjacent sugar by a phosphodiester bridge. The *variable part* of DNA is its *sequence of four kinds of bases (A, G, C, and T).* The corresponding nucleotide units are called *deoxyadenylate, deoxyguanylate, deoxycytidylate,* and *deoxythymidylate.* The structure of a DNA chain is shown in Figure 4-2.

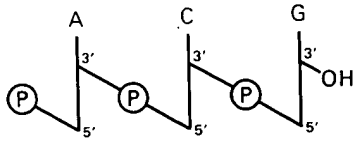
The structure of a DNA chain can be concisely represented in the following way. The symbols for the four principal deoxyribonucleosides are



The bold line refers to the sugar, whereas A, G, C, and T represent the bases. The Ⓟ within the diagonal line in the diagram below denotes a phosphodiester bond. This diagonal line joins the end of one bold line and the middle of another. These junctions refer to the 5′-OH and 3′-OH, respectively. In this example, the symbol Ⓟ indicates that deoxyadenylate is linked to deoxycytidine by a phosphodiester bridge. Specifically, the 3′-OH of deoxyadenylate is joined through a phosphoryl group to the 5′-OH of deoxycytidine.



Now suppose that deoxyguanylate becomes linked to the deoxycytidine unit of this dinucleotide. The resulting trinucleotide can be represented by



An even more abbreviated notation for this trinucleotide is pApCpG or ACG.

A DNA chain has polarity. One end of the chain has a 5′-OH group and the other a 3′-OH group that is not linked to another nucleotide. By convention, the symbol ACG means that the unlinked 5′-OH group is on deoxyadenosine, whereas the unlinked 3′-OH group is on deoxyguanosine. Thus, *the base sequence is written in the 5′ → 3′ direction.* Recall that the amino acid sequence of a protein is written in the amino → carboxyl direction. Note that ACG and GCA refer to different compounds, just as Glu-Phe-Ala differs from Ala-Phe-Glu.

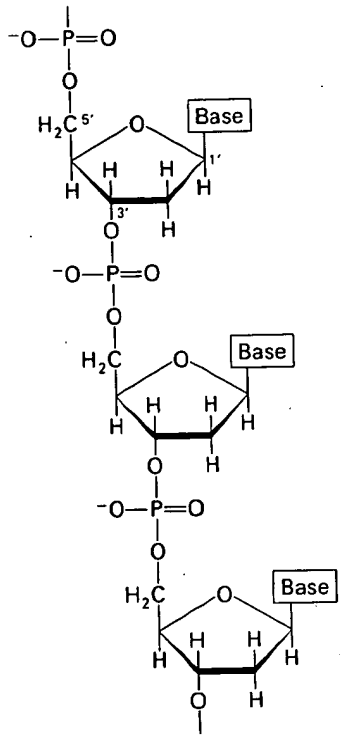


Figure 4-2
Structure of part of a DNA chain.

TRANSFORMATION OF PNEUMOCOCCI BY DNA REVEALED THAT GENES ARE MADE OF DNA

The pneumococcus bacterium played an important part in the discovery of the genetic role of DNA. A pneumococcus is normally sur-